

REVIEW ARTICLE

Interpleural block – part 1

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Summary

Interpleural blockade is effective in treating unilateral surgical and nonsurgical pain from the chest and upper abdomen in both the acute and chronic settings. It has been shown to provide safe, high-quality analgesia after cholecystectomy, thoracotomy, renal and breast surgery, and for certain invasive radiological procedures of the renal and hepatobiliary systems. It has also been used successfully in the treatment of pain from multiple rib fractures, herpes zoster, complex regional pain syndromes, thoracic and abdominal cancer, and pancreatitis. The technique is simple to learn and has both few contra-indications and a low incidence of complications. In the first of two reviews, the authors cover the history, taxonomy and anatomical considerations, the spread of local anaesthetic, and the mechanism of action, physiological, pharmacological and technical considerations in the performance of the block.

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Interpleural blockade is the technique of injecting local anaesthetic into the thoracic cage between the parietal and visceral pleura to produce ipsilateral somatic block of multiple thoracic dermatomes. There is evidence that it also produces pain relief by spread of local anaesthetic bilaterally to block both the sympathetic chains and the splanchnic nerves. It is effective in treating unilateral surgical and non-surgical pain from the chest and upper abdomen in both the acute and chronic settings. Local anaesthetic solutions can be administered as single or intermittent boluses, or as continuous infusions via an indwelling interpleural catheter. It has been shown to provide safe, high-quality analgesia after cholecystectomy, thoracotomy, renal and breast surgery, and for certain invasive radiological procedures of the renal and hepatobiliary systems. It has also been used successfully in the treatment of pain from multiple rib fractures, herpes zoster, complex regional pain syndromes (CRPS), thoracic and abdominal cancer, and pancreatitis. The technique is simple to learn and has both few contra-indications and a low incidence of complications. Interpleural blockade has not been widely adopted by the anaesthetic community largely because of concerns about pneumothorax and local anaesthetic toxicity. However,

recent improvements in technique that enhance its safety, and increased experience with this form of treatment, suggest that a revisit to this interesting and useful technique of regional anaesthesia would be of value. In the first of this two-part review, we discuss the history, taxonomy and anatomical considerations, the spread of local anaesthetic, and the mechanism of action, physiological, pharmacological and technical considerations in the performance of the block.

History

Interpleural injection was first described by Mandl in 1947 when he administered 6% phenol into the interpleural space of experimental animals without any evidence of pleural irritation or necrosis. Interest resurfaced in 1978, when Wallach used this space for therapy with tetracycline and lidocaine for malignant pleural effusions [2]. The concept of the injection of local anaesthetic into the interpleural space for the provision of pain relief was first presented by Kvalheim and Reiestad [3] in 1984, and was published in 1986 by Reiestad and Strømskag [4] as a means of treating pain after open cholecystectomy, kidney surgery and breast surgery.

Before this, interest had focused on the use of multiple intercostal nerve blocks for these indications. Nunn and Slavin showed in a cadaver study that local anaesthetic from a single injection around one intercostal nerve gained access to other intercostal nerves in adjacent spaces above and below the injection site. This occurred through both the intercostal and the subpleural spaces [5]. O'Kelly and Garry used this knowledge about the spread of local anaesthetic to provide continuous analgesia for pain relief after multiple rib fractures with a single intercostal catheter and intermittent drug administration [6]. This approach was also described in a series of patients undergoing gallbladder and kidney surgery [7, 8]. Kvalheim and Reiestad attempted to demonstrate fluid spread by injecting local anaesthetic and radiological contrast medium through a catheter placed in an intercostal space. They observed that, in addition to providing excellent analgesia, the radiological contrast medium spread over the lung surface, prompting them to conclude that the catheter was actually located interpleurally. The authors therefore decided to reproduce this analgesia by deliberately placing the catheter in the interpleural space. They thus exploited a technical mistake to achieve a positive result and developed a new regional anaesthetic technique [9].

Taxonomy

The original paper uses the term interpleural block, implying the injection of local anaesthetic solution into the potential space between the parietal and visceral layers of the pleura. Some authors prefer the term intrapleural because the pleura are one structure embryologically, and the solution is deposited within this structure [10]. Others feel that the latter term is unsatisfactory because it implies actual injection within or into the pleural layer itself [11]. Baumgarten suggested pleural block or pleural analgesia [12]. All these terms are used interchangeably. Intercostal is the more frequently used term in the literature and we have therefore used this term in this review.

Anatomical considerations

It is essential to review the literature relating both to the intercostal and interpleural space for a thorough understanding (Fig. 1). Recent studies suggest a greater variability in the anatomy of the intercostal space than that suggested in classic texts. Classically, the space has been described as having three muscle layers; *intercostales externi*, *interni* and *intimi*. *Intercostalis intimi* runs obliquely downwards and backwards, joining the internal surfaces of the adjacent ribs. Some fibres may bridge more than one intercostal space to be inserted into the second

or third rib. *Intercostales intimi* separates the neurovascular bundle from the parietal pleura. The intercostal nerve is classically described as running under the shelter of the intercostal groove, and is situated below the intercostal vein and artery.

Nunn and Slavin [5] performed detailed studies in cadavers. At the sixth intercostal space, 7 cm from the posterior midline, the external intercostal muscle was of variable thickness but well developed and was bound internally by the posterior intercostal membrane, the sturdy, aponeurotic extension of the internal intercostal muscle. However, the innermost intercostal muscle, the *intercostales intimus*, was 'a flimsy structure composed of several fascicles through which injected India ink passes freely to reach the subpleural space'. The nerves, arteries and veins were consistently found in the tissue plane deep to the posterior intercostal membrane and superficial to the *intercostales intimus* muscle, with no fixed relationship to the ribs above or below. The intercostal nerves were found to run 'as three or four separate bundles with no single neural sheath' and with considerable variation in size and relationship to the associated intercostal arteries and veins. Hardy concurred with these findings. In 30 cadavers, the second to eleventh intercostal nerves were dissected and were found to occupy the classically described subcostal position in only 17% of cases [13].

In the embryo, the pleura is a layer of mesothelium into which each lung bud grows and expands. The original coelomic cavity is reduced to a slit-like space called the pleural cavity. The parietal layer lines the thoracic wall, the thoracic surface of the diaphragm and the lateral aspect of the mediastinum, and extends into the root of the neck to line the suprapleural membrane at the thoracic inlet. The visceral layer completely lines the outer surfaces of the lungs and extends into the depths of the interlobar fissures. The two layers become continuous with one another by means of a cuff of pleura that surrounds the structures entering and leaving the lung at the hilum. The two layers of pleura are separated by a distance of 10–20 μm . The space has a surface area of about 2000 cm^2 in a 70-kg man and contains 0.1–0.2 ml.kg^{-1} of pleural fluid, permitting the two layers to move over each other with minimum friction. The parietal pleura is thinner than the visceral layer, and contains stomata of 2–12 μm diameter between its mesothelial cells, suggestive of a membrane capable of fluid transport [14]. The diffusion of local anaesthetic from the pleural space to the intercostal nerves is limited by uptake of drug by the visceral pleura. The rapidity and extent of absorption is unpredictable after pleural injury, disease or inflammation. The parietal pleura has the following nerve supply: the costal pleura is segmentally supplied by the intercostal nerves, the mediastinal pleura

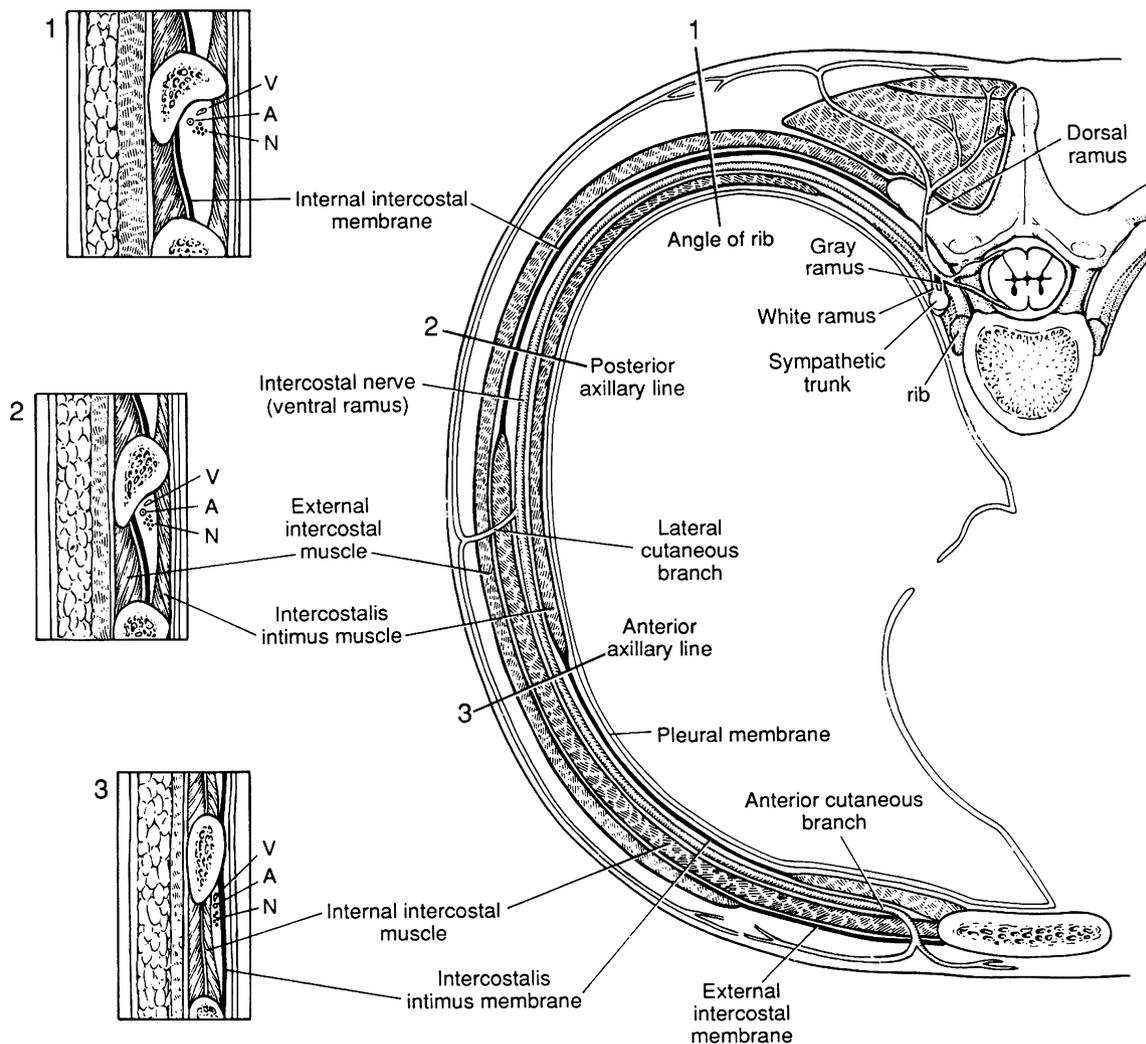


Figure 1 The anatomy of the intercostal space.

is supplied by the phrenic nerve and the diaphragmatic pleura is supplied over the domes by the phrenic nerve and around the periphery by the lower five intercostal nerves. The visceral pleura covering the lung receives an autonomic vasomotor supply but has no sensory innervation. Strömskag and Kleiven suggested that a volume of 3–5 ml of local anaesthetic would be confined only to the injected intercostal space but that the administration of a larger volume of 20 ml could extend subpleurally to up to five adjacent intercostal spaces [9] (Fig. 2).

In his study in cadavers, Murphy [15] demonstrated the spread of India ink from the injected intercostal space to adjacent intercostal spaces above and below. The spread was shown to occur medially to reach the paravertebral space in only 50% of the studies. In contrast, Mowbray et al. found that methylene blue injected through an intercostal catheter almost invariably spread to the

paravertebral space and cited this as the reason that analgesia extends over several dermatomes [16]. Just how the fluid injected into the interpleural space reaches adjacent neural structures and how interpleural blockade can be used to treat pain arising from structures both above and below the diaphragm has been the subject of much interest (Fig. 3).

Cadaver studies have shown that interpleurally injected India ink diffuses through the parietal pleura to the subpleural space and backwards to multiple intercostal nerves [14]. Animal studies also support this spread [17, 18], the dye almost completely covering the chest wall, lung and diaphragm, and tending to pool in the interpleural paravertebral area (not the paravertebral space as used for the thoracic paravertebral block) which is dorsal to the parietal pleura and hence extra-pleural. Further evidence regarding the spread comes from a study

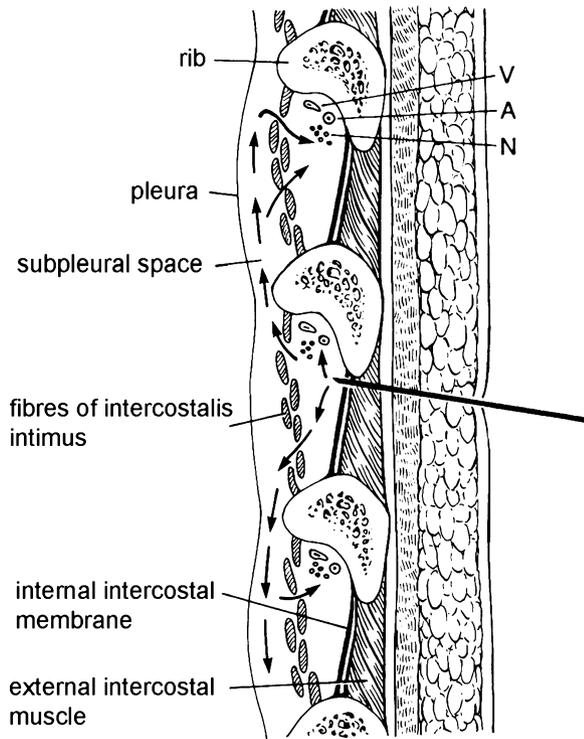


Figure 2 The paths taken by fluid injected into the intercostal space.

that used computerised tomography to investigate the behaviour of interpleural local anaesthetic injections in 21 subjects after open cholecystectomy [19]. Bupivacaine 0.375% 20 ml mixed with 10 ml of contrast medium was used for the injection. The study found that most of the

fluid injected collects at the lowest point of the pleural cavity in a gravity-dependent manner, and so spread will vary with body position. In the supine position, the mean distribution in a cranio-caudal direction was from the T3 level to L1, and in the lateral position it was from T5 to L1. Although the paravertebral regions of the interpleural space were covered, there was no spread seen in any case to the epidural or paravertebral spaces.

However, in addition to intercostal nerve blockade, clinical evidence of analgesic effects suggest that other neural structures in close proximity can also be affected by interpleural block. Clinical studies reporting relief of sympathetically mediated pain point to autonomic blockade being produced by this block [20–22]. In the lateral position with the operative side up, the main fluid collection is against the mediastinum, supporting the suggestion that the technique can result in blockade of the thoracic sympathetic chain and the splanchnic nerves [19]. These structures are separated from the interpleural space by the parietal pleura alone. Where the standard supine and lateral positions are used, the uppermost part of the thoracic sympathetic chain is spared. The first thoracic sympathetic ganglion, from which the sympathetic fibres destined to the upper limbs (ganglia 1–4) and to the heart (ganglia 1–5) originate, is not blocked. This is supported by vasoconstriction seen in the arms and by the relative stability of blood pressure and heart rate. Vasoconstriction is also observed in the lower limbs, signifying that the blockade does not affect the lumbar sympathetic chain. It is suggested that this vasoconstriction above and below the level of block compensates for the vasodilation in the splanchnic area. This is mediated through the arterial

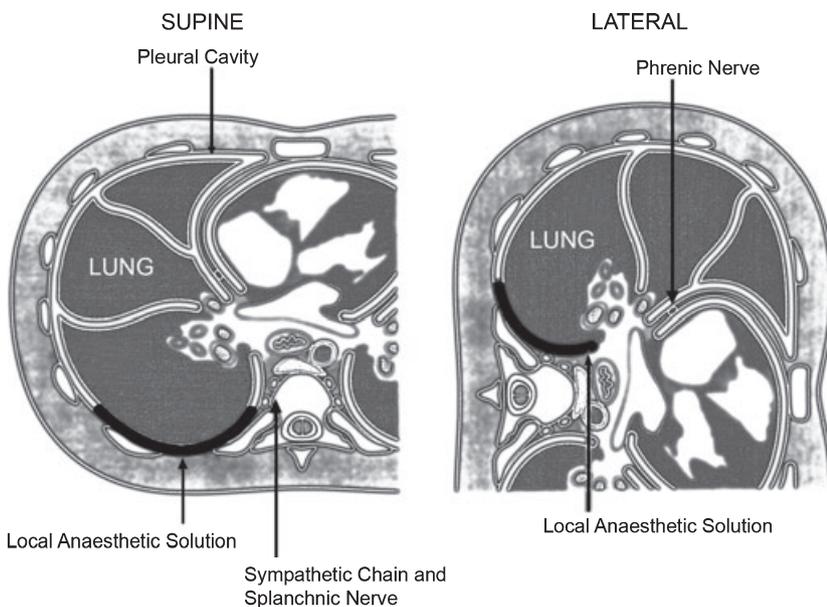


Figure 3 The effect of gravity on the spread of local anaesthetic solution injected into the intrapleural space.

baroreceptors in the aortic arch, as observed with an epidural block, with the difference that the integrity of the intervening spinal cord permits a vasoconstrictive response in lower limbs [19, 23]. Spread of local anaesthetic can be encouraged in a cephalad direction by using a 20° head-down position to achieve blockade of ipsilateral stellate and upper thoracic ganglia, and brachial plexus. This is discussed later in this review.

Based on a study using infrared telethermography, there is a suggestion that injection of local anaesthetic on one side, apart from causing an ipsilateral somatic block, can result in bilateral block of the thoracic sympathetic chains and the splanchnic nerves located between them and in front of the spinal column [24]. Ramajoli et al. [24] performed a unilateral block with bupivacaine in 15 patients suffering from benign or neoplastic pain of thoracic or abdominal origin. Catheters were placed on the same side as the thoracic or abdominal somatic pain and on the opposite side of maximally reported thoracic or abdominal visceral pain. Using infrared telethermography, they detected a uniform bilateral cutaneous temperature increase in the affected thoracic dermatomes and decreased temperatures in the upper and lower limbs in all the cases. The authors hypothesised that reflex vasoconstriction occurs in areas unaffected by the block in compensation for the region of sympathetic blockade. The exact mechanism of bilateral thoracic sympathetic block after unilateral injection is not known, although a greater negative mediastinal pressure may facilitate bilateral spread. The authors felt that this was the reason for a marked reduction in or disappearance of diffuse or unilateral visceral pain after the administration of local anaesthetic, regardless of the side of catheter placement.

In summary, it has been suggested that local anaesthetic solution diffuses outwards, producing a block of multiple intercostal nerves, the sympathetic chain of the head, neck and upper extremity, the brachial plexus, the splanchnic nerves, the phrenic nerves, the coeliac plexus and ganglia [23]. As the injected local anaesthetic diffuses out through both the layers of pleura, direct local effects on the diaphragm, lung, pericardium and peritoneum may contribute to some of the analgesic activity.

Effects on pulmonary function

The effect of interpleural analgesia on pulmonary function has been the focus of several studies, as blockade of intercostal nerves (and potentially the phrenic nerve) might be expected to affect respiratory muscle strength. Murphy demonstrated significant improvements in peak flow in patients with rib fractures and after cholecystectomy with continuous intercostal nerve blockade managed with intermittent boluses of bupivacaine [7, 8].

Other studies have reported improved respiratory function after interpleural block for postoperative pain [25–29]. Van Kleef et al. [29] compared bupivacaine 0.25% with adrenaline and 0.5% with adrenaline given as interpleural boluses followed by continuous infusions in patient undergoing surgery with a flank incision. They reported a significant improvement in forced expiratory volume in 1 s (FEV₁) and forced vital capacity (FVC), and a decreased morphine requirement, which was similar with both local anaesthetic concentrations used. They went on to recommend the lower strength for these patients. Another study concluded that, although interpleural block did not significantly change lung function or inspiratory muscle strength after open cholecystectomy, it induced a slight decrease in abdominal wall muscle strength [30]. Oxorn et al. studied pulmonary function, comparing interpleural bupivacaine with intramuscular pethidine after open cholecystectomy [31]. Their findings are in direct contrast, showing intramuscular pethidine to be superior in terms of postoperative pulmonary mechanics. Ballantyne et al. showed that the block decreases the incidence of postoperative pulmonary complications, although not statistically significantly so, in a meta-analysis of postoperative analgesic techniques. They also concluded that surrogate measures of pulmonary function, i.e. FEV₁, FVC and peak expiratory flow rate (PEFR), could not be used to predict outcomes or complications [32]. Kastrissios et al. also reported early normalisation of bowel function and an early return to unaided mobilisation with interpleural block [26]. In summary, it would seem that interpleural block has no clinically significant adverse effect on respiratory muscle function, and is likely to be beneficial in the presence of painful conditions compromising pulmonary function. Although this block has been successfully used in patients with cystic fibrosis [33], in view of the above negative study and the possibility of phrenic nerve paralysis, however uncommon, a careful consideration must be given to its use, especially where a long-term or a bilateral block is being contemplated and in those with borderline respiratory function or with neuromuscular disease.

Technique

The first description of a technique for interpleural analgesia employed a 16-G Tuohy needle and a well-wetted and freely moving air-filled glass syringe. The block was performed at the end of surgery with the patient in the lateral position with the operated side uppermost. A site 10 cm from the posterior midline in the eighth intercostal space was chosen. Following skin puncture, the needle and syringe were advanced together

through the intercostal space towards and then through the parietal pleura. Puncture of this layer is often signified by a 'click'. Immediately upon entering the interpleural space the negative pressure therein would 'elegantly surge the plunger of the syringe forward'. The syringe was removed and a 5–6-cm length of an epidural-type catheter quickly inserted through the needle into the pleural space [3].

This could be described as a 'passive' loss of resistance technique or negative pressure technique. Some anaesthetists use the traditional 'loss of resistance' technique, where a gentle pressure is exerted on the plunger as the needle and air or fluid-filled syringe assembly is advanced through the intercostal space. A potential disadvantage is that a false loss of resistance can occur anywhere in the intercostal space, with the puncture of parietal pleura or when the needle is advanced too far into the lung parenchyma itself, and for this reason this should be strictly avoided [34].

The technique for identifying the interpleural space should rely on the identification of negative pressure within the space. Pleural pressures are negative throughout the normal respiratory cycle and hence key to successful identification of the space. In contrast to this, a study using epidural catheters for continuous intercostal and interpleural local anaesthetic blockade has shown the intercostal pressure to be positive during the expiratory phase, an important differentiating feature between the two blocks [35]. In an anaesthetised spontaneously breathing patient the needle advancements are undertaken in the expiratory phase, whereas in a paralysed and ventilated patient the needle is advanced at the end of exhalation with the ventilator disconnected. An awake patient should be advised to hold their breath at the end of exhalation and should be warned of the feeling of a sharp 'twinge' when the needle pierces the pleura.

The negative interpleural pressure has been identified with a passive suction of air-filled syringe [3], a fluid-filled syringe [36], deflation of a balloon [37], a falling column of fluid [38, 39], suction of a hanging drop from the hub of the needle [40], saline infusion [41], a continuous saline flow [42], or electronic devices that detect negative pressure [43], and is indicated by an unobstructed passage of the catheter. O'Leary et al. [1] suggested that electronic devices may prove useful adjuncts for identification of the space, especially in the obese and those with pleural disease, although presently there are no new data available to support this.

False endpoints remain a possibility with some of the techniques, and introduction of air into the pleural space is difficult to avoid if the Tuohy needle is open to air at any time, even for a short period, to enable connection of a syringe or to allow the passage of a catheter. As much as

20 ml of air may be entrained, causing air pockets, which may result in a patchy block [1]. Introducing air may also be hazardous if nitrous oxide is to be used as part the anaesthetic technique. Scott [41] used the 'saline infusion technique' to identify negative pressure in the interpleural space. This is a suitable technique for single bolus injections and also permits catheter placement through a catheter sheath adaptor. As a catheter sheath adaptor is not routinely available, authors recommend the 'continuous saline flow' technique to avoid air entrainment during catheter placement. We perform the block in the lateral position approximately 8–10 cm from the dorsal midline. The needle insertion site is prepared and infiltrated with local anaesthetic if appropriate. A 500-ml bag of saline with an infusion set is positioned approximately 60 cm above the level of the patient and the infusion set is attached to the side port of a standard three-way connector ensuring sterility, and primed with the saline (Fig. 4). The other port is kept closed. The Tuohy needle is inserted through the skin and connective tissue until the rib is touched. The stylet is then removed and the three-way connector is attached to the hub of the Tuohy needle (Fig. 5).

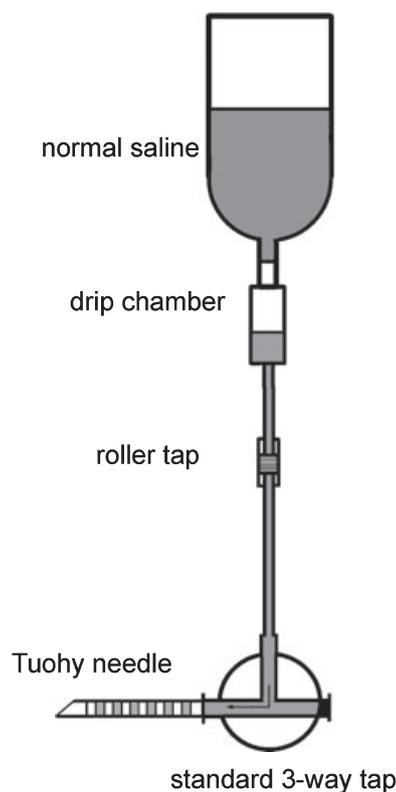


Figure 4 Arrangement of equipment for insertion of an intra-pleural catheter.

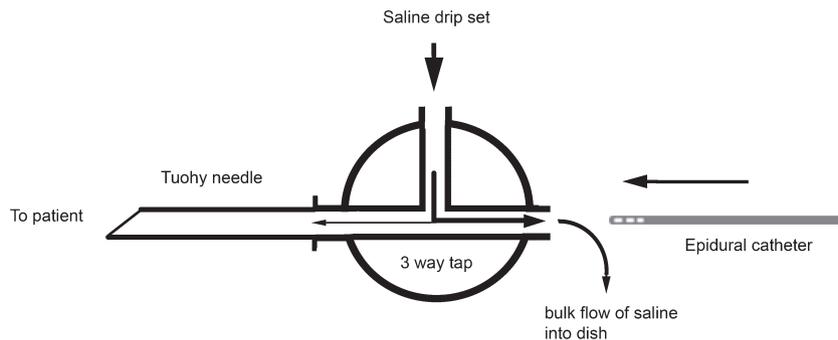


Figure 5 After insertion of the Tuohy needle, a catheter is passed through the open three-way tap and freely flowing saline.

The roller tap of the giving set is then fully opened. At this point, a few drops are usually seen in the drip chamber of the giving set, but free flow will not occur. Controlled ventilation is stopped and the breathing system is disconnected from the patient before the needle is advanced any further; if the patient is breathing spontaneously, all further movements of the needle are carried out in the expiratory phase. The anaesthetist then walks off the upper border of the rib, remembering to avoid angling the needle and accidentally entering the neurovascular bundle in the intercostal groove of the rib above. Further advance through the intercostal space is accompanied sometimes by a brisk flow of saline drops. This flow sometimes slows down just before the parietal pleura is punctured, which is associated with, and indicated by, a sudden and free flow of saline in the drip chamber due to the negative pressure in the space. We rely on this change in character of saline flow, which indicates negative pressure, rather than on a 'clicking' sometimes felt on puncturing the pleura. With the guiding hand still gripping the needle and firmly rested on the patient's torso, the connector is then opened to all three ports whereupon saline preferentially flows out towards the operator through the wide bore of the three-way connector rather than through the narrow bore needle into the chest (Fig. 4c).

The continuous flow of saline creates a pressure of at least 60 cmH₂O at the connector and prevents air entrainment. A standard epidural catheter is threaded through the jet of saline into the pleural cavity through the three-way connector and the needle. Approximately 5–10 cm of catheter is inserted into the interpleural space. The saline flow is continued until the needle is fully withdrawn from the chest [42].

Interpleural block can be performed with the patient flat or semirecumbent in either the supine or lateral position. Catheter insertion permits administration of repeat boluses or a continuous infusion regimen. Various approaches to the space have been used, which include the anterior axillary line [44], mid-axillary line [41, 45],

the posterior axillary line [24], a site about 8–10 cm from the dorsal midline [42], and even anteriorly in the second intercostal space in the mid-clavicular line [24]. A site is chosen for needle insertion, ideally where the intercostal space and adjacent rib below are easily palpable. In general, the fourth to eighth intercostal spaces in the mid to anterior axillary line are used in the supine patient. Although not as convenient, the lateral position allows a more posterior needle insertion point, with the theoretical advantage of depositing the local anaesthetic into the paravertebral region of the interpleural space where the intercostal nerves and sympathetic chain are most superficial with regard to the parietal pleura, as discussed above. Strømskag et al. showed that collection in the paravertebral area occurs whether the patient is supine or lateral [19]. Iwama [44] performed the block with a 16-G Tuohy needle at the fourth intercostal space in the anterior axillary line and directed radio-opaque catheters either towards the apex or towards the base of the pleural space. The extent of the spread of the injected radioisotope and local anaesthetic was checked with a gamma camera and the extent of hypo-aesthesia to a cold stimulus. He recommended that the catheter should be inserted toward the apex of the pleural space and the local anaesthetic should be administered with the patient supine to obtain the best pain relief in the chest.

Interpleural block for postoperative analgesia can be performed after induction of anaesthesia. If performed after induction, it will decrease intra-operative anaesthetic and analgesic requirements, and haemodynamic responses to surgery [46]. The block can also be easily performed at the end of surgery, with the patient still anaesthetised and either mechanically ventilated or breathing spontaneously after reversal of the neuromuscular block. This provides good quality analgesia with opioid sparing and without the inherent risk of neuraxial injury to an anaesthetised patient, a concern with an epidural.

Interpleural catheters are most commonly placed percutaneously through the needle, although they may also be placed during thoracotomy by the surgeon.

Reber and Scheidegger have suggested inserting an epidural catheter for interpleural block via a chest tube under direct visual guidance [47].

The position of the patient can be optimised to facilitate local anaesthetic spread and block appropriate neural structures to achieve desired clinical effects. If blockade of the upper sympathetic ganglia is desired, as in the treatment of CRPS [20] or ischaemia affecting the upper limb [48], then the patient should be positioned with the affected side uppermost and with a 20° head-down tilt to encourage cephalad spread in the paravertebral area. This position should be maintained for 30 min after injection to give the local anaesthetic time to penetrate the tissues. Reiestad et al. [20] reported pain relief, lack of sweating, increased hand temperature and ipsilateral Horner's syndrome with this positioning. As O'Leary et al. suggests, this position, apart from unilaterally blocking cervical and superior thoracic segments of the sympathetic chain, would also cause partial blockade of the ipsilateral brachial plexus as demonstrated by hypo-aesthesia in C3–T1 dermatomes and motor weakness of shoulder, arm and forearm [1]. Diffusion of local anaesthetic to the ipsilateral brachial plexus contributes to relief of these head and neck and upper extremity pain syndromes. Although there is a theoretical risk of affecting cardiac sympathetic nerves by encouraging cephalad spread within the pleural space, this has not been reported and cardiovascular stability is well maintained. For surgical anaesthesia for unilateral breast tumour resection, the lateral position on the affected side and a head-down tilt maintained for about 30 min should produce unilateral block of the T1–T9 dermatomes with complete skin anaesthesia. For managing postoperative pain and chest trauma, the lateral position with a 20° head-up tilt and the affected side uppermost during injection over 5–6 min should achieve a blockade of both the sympathetic chain and intercostal nerves of the affected side. The patient is turned supine after injection [1]. In our experience, we use a posterior approach for catheter placement and perform injections with the patient supine while moving the patient into head-up and head-down positions to obtain a somatic block of the T1–T12 dermatomes, providing good pain relief for gall bladder, kidney and breast surgery, including axillary node clearance.

Consent for the procedure should be obtained to the published standard [49]. The block should be performed in an appropriate area which offers privacy, good lighting and ensures sterility, and with oxygen, monitoring and resuscitation drugs and equipment readily available [50]. A trained anaesthetic assistant should be present, and full aseptic precautions observed.

The focus of many studies has been the provision of safe dosing regimens, which provide a balance of good quality

Table 1 Volumes and concentrations of bupivacaine reported for use intrapleural analgesia.

Volume	Concentration	References
Single injections		
10 ml	0.25%	61*
10 ml	0.5%	62
0.4 ml.kg ⁻¹	0.5%	56*
20 ml	0.25%	24, 28*, 52*, 63*
20 ml	0.375%	19, 52*, 57*, 64
20 ml	0.5%	4, 24, 26*, 27*, 30*, 31*, 46, 52*, 54*, 65*, 66, 67*, 68*
30 ml	0.25%	69
30 ml	0.5%	70, 71*, 72, 73*
Infusions		
0.125 ml.kg ⁻¹ .h ⁻¹	0.25%	56*
5 ml.h ⁻¹	0.25%	29*, 63
5–10 ml.h ⁻¹	0.25%	9*
6 ml.h ⁻¹	0.375%	64
5 ml.h ⁻¹	0.5%	29*

*With adrenaline 1 : 200 000.

and prolonged pain relief with acceptable plasma local anaesthetic concentrations. Reiestad and Strømskag [4] administered a single bolus of bupivacaine 0.5% with adrenaline 20 ml via an interpleural catheter at the end of breast surgery, renal surgery and cholecystectomy for the management of postoperative pain. Of the 81 patients studied, 78 required no additional analgesic measures during the first 24 h after surgery. The duration of analgesia ranged from 6 to 27 h, with a mean duration of about 10 h. However, other studies have shown only 3–6 h of analgesia from each bolus despite the use of larger doses of local anaesthetic than were originally described [27, 28, 51]. Table 1 lists some published dosage regimens.

As for concentration, bupivacaine 0.25% 20 ml would appear to be as effective in relieving pain after open cholecystectomy as equal volumes of bupivacaine 0.375% and 0.5%, although decreasing the dose decreases the duration of analgesia [52]. The median time from the interpleural injection of 20 ml of bupivacaine with adrenaline 1 : 200 000 0.25%, 0.375% and 0.5% to the administration of supplementary analgesia was reported to be 4 h 20 min, 6 h 0 min and 7 h 45 min, respectively. Higher interpleural doses of bupivacaine with adrenaline 1 : 100 000 0.5% 30 ml have been used, with blood levels remaining in a safe range in all but one patient, who was deemed to have had inflamed pleura from recent pneumonia and who rapidly developed symptoms of central nervous system toxicity [51]. Similar volumes of bupivacaine 0.75% have been found to produce high plasma drug concentrations and are not recommended [53]. When the literature is assessed with regards to the volume of local anaesthetic administered into the inter-

pleural space, boluses from 8 to 40 ml have been used with good analgesic effects. When bupivacaine 0.5% 20 ml was compared to 40 ml of a 0.25% solution, little difference was seen in terms of onset time, extent and duration of analgesia [54]. It is suggested that bolus doses of 30 ml of bupivacaine 0.5% are safe and effective when administered no more frequently than every 6 h [55].

As an alternative to single or intermittent local anaesthetic boluses, indwelling catheters may be used for continuous infusions, which are safe, effective and less labour-intensive. This has been found to produce better postoperative analgesia and plasma levels well below toxic levels in some studies [56, 57], although not all studies are in agreement with this. Laurito et al. [56] used an infusion of bupivacaine 0.25% at a rate of $0.125 \text{ ml.kg}^{-1}.\text{h}^{-1}$ and found that it provided better analgesia and significantly lower plasma concentrations after open cholecystectomy when compared to 6-hourly boluses of 0.4 ml.kg^{-1} of bupivacaine 0.5% with 1 : 200 000 adrenaline. Van Kleef et al. [57] compared infusion regimes of 5 ml.h^{-1} of bupivacaine 0.25% and 0.5%, both with 1 : 200 000 adrenaline, started after a loading dose of 21 ml of the same solution in patients who underwent surgery with unilateral flank incisions. They reported comparable analgesic efficacies in both, but a lower bupivacaine plasma concentration in the group that received the lower strength solution [29]. Strömskag and Kleiven [9] favour infusion over intermittent boluses, and for adults recommends a loading bolus of bupivacaine 0.5% with 1 : 200 000 adrenaline 20 ml followed by infusion of bupivacaine 0.25% with adrenaline at a rate of $5\text{--}10 \text{ ml.h}^{-1}$. Whilst most experience comes from the use of this technique in adults, infusions are also used by some centres with good effect in infants and children for analgesia after thoracic surgery [58, 59]. With regards to duration of catheter placement, there are reports of interpleural catheter use for 10 days in patients with multiple rib fractures [60], for 130 days in patient with cancer [23] and for 9 months in a patient with chronic pancreatitis [9]. Local anaesthetic rotation, similar to opioid rotation, alternating bupivacaine and ropivacaine, has been used to overcome the problem of tachyphylaxis [9].

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